Drug Companies and the NIH

How the pharmaceutical industry is reaping billions off of taxpayer-funded research and development

Compiled by the Office of Rep. Bernard Sanders

The NIH and Taxpayer Funded R&D: An Overview

Right now, the federal government gives away billions of dollars worth of taxpayer-financed intellectual property to huge, profitable pharmaceutical companies.

The National Institutes of Health are the jewel of American science, producing lifesaving drugs of enormous value to our nation and the world. From 1955 to 1992, for example, 92% of drugs approved by the FDA to treat cancer were researched and developed, with help from NIH. However, much of the financial value of these drugs is given away to pharmaceutical corporations in an outrageous example of corporate welfare.

Currently, once NIH has successfully developed a new drug it signs over monopoly commercial rights to large pharmaceutical companies which can - and do - charge American consumers as much as they want. In the case of Levamisole, a profitable pharmaceutical took exclusive rights to a drug with NIH-discovered anti-colon cancer properties and charged consumers over one hundred times its cost.

It is absurd that Americans must pay twice for lifesaving drugs, first as taxpayers to develop the drug and then as consumers to pad pharmaceutical profits. These costs fall hardest on those least able to bear the burden, such as cancer patients, AIDS patients and senior citizens, nearly half of whom must pay the full cost of prescription drugs out of pocket. This is particularly outrageous because, unlike the Americans who must bankrupt themselves to get lifesaving medicines, the pharmaceutical industry is extremely healthy and hardly in need of taxpayer support. From 1988 through 1995, pharmaceuticals surpassed all other Fortune 500 industries in profit rates, and they have ranked in the top two for 31 of the past 39 years.

The Sanders amendment requires the NIH to insure that drugs developed at taxpayer expense are provided to the public on reasonable terms. This anti-corporate welfare legislation is not a radical proposal; former NIH Director Bernadine Healy called pharmaceutical overpricing of taxpayer-financed drugs “inhuman,” and President Bush instituted a reasonable pricing clause for drugs developed largely with government resources at NIH.

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HISTORY OF REASONABLE PRICING LEGISLATION

1980s: Under the Reagan/Bush Administrations, the NIH required drug companies to charge a "fair and reasonable price" for products originally developed with taxpayer-funded research and development.

1995: Clinton Administration NIH Director dropped the reasonable pricing requirement.

1995: Sanders offers first version of reasonable pricing bill, garnering 140 bipartisan votes

1996: Sanders offers second reasonable pricing bill, garnering 180 bipartisan votes

2000: Sanders offers amendment requiring the NIH to ensure that drugs developed at taxpayer expense are made available to the public on reasonable terms. The amendment passes by a vote of 313-109.

THE ROLE OF NIH IN DRUG DEVELOPMENT

Federal government is a major player in drug research: The Federal government funds about 36% of all U.S. medical research (Congressional Joint Economic Committee Report, May, 2000)

Major drugs have been developed with taxpayer-funded research: Of the 21 most important drugs introduced between 1965 and 1992, 15 were developed using knowledge and techniques from federally funded research. Of these, NIH research led to the development of 7 drugs to treat patients with cancer, AIDS, hypertension, depression, herpes and anemia

Taxpayer funded research is becoming more important: A study of 32 drugs introduced before 1990 found that without the contributions of government laboratories and non-commercial institutions, approximately 60% of the drugs would not have been discovered or would have been delayed. "This suggests public sector research is becoming more important over time" (Maxwell and Eckhart – 1990)

DRUGS DEVELOPED WITH TAXPAYER FUNDS

Tamoxifin - Major breast cancer drug which was the product of 140 NIH sponsored clinical trials. Currently, Americans pay approximately, $241 per treatment, while in Canada the price is about $34

Zovirax – Drug which treats the herpes simplex virus utilized NIH-funded research to purified virus-specific enzymes that were crucial in development of the drug.

AZT - This major AIDS treatment drug was screened by the National Cancer Institute. Patients with AIDS pay great amounts for AZT treatment, with many poor AIDS patients cannot afford treatment.

Capoten - The popular blood pressure medication was developed using key NIH-funded research that targeted the enzyme that causes high blood pressure.

Platinol - This drug was developed by the National Cancer Institute, and has had great success to treat and cure individuals with testicular, cervical, and ovarian cancer.

Epogin – Drug which has extended the lives of countless End Stage Renal Disease patients was developed by the National Institute of Diabetes, Digestive, and Kidney Diseases.

Prozac - Antidepressant was made possible by the research that discovered the brain chemical, serotonin.

Taxol – Cancer drug was developed with $32 million in federal funding, then given to Bristol-Myers Squibb which now charges $10,000 for a year's supply.

Xalatan – A best-selling drug to treat glaucoma was originally developed with a $4 million NIH grant

Associated Press

June 13, 2000

House Votes on Drug Prices

By Alan Fram

The House voted Tuesday to require pharmaceutical companies to charge reasonable prices for products they develop as a result of federally financed basic research.

Though it is unclear if the provision will ever make it into law, the 313-109 vote underlined the political potency this election year of accusing drug companies of charging high prices.

In a mark of the effort's wide-ranging appeal, the measure was sponsored by Rep. Bernard Sanders of Vermont, a socialist and one of the most liberal members of Congress, and co-sponsored by Rep. Dana Rohrabacher, R-Calif., one of the House's most conservative members. It received a majority of Democratic and Republican votes.

The provision would require the National Institutes of Health to obligate companies using institute research to charge prices "on reasonable terms" for any pharmaceuticals they develop, said Sanders spokesman David Sirota. The institutes, which are federal agencies, perform biomedical research and give grants to university and other scientists.

The provision would not apply to such products already on the market, Sirota said. These include tamoxifen, used for fighting breast cancer, the anti-AIDS drug AZT, and taxol, another anti-cancer drug.

"This is nothing more than asking a fair return for the taxpayers of this country for their investment" of billions of dollars annually in biomedical research, Sanders said.

Drug companies argue that the prices they charge are justified by the billions they must invest in producing effective new drugs.

Rep. John Porter, R-Ill., opposed the provision, saying the basic biomedical research performed by the National Institutes of Health is available to all companies to use. Those that develop successful products by building on that research are "simply adding to a body of knowledge that is available to all companies everywhere," he said.

The language was attached to a $339 billion measure financing health, education and labor programs for the coming fiscal year.

The New York Times

April 23, 2000

Birth of a Blockbuster: Drug Makers Reap Profits On Tax-Backed Research

By Jeff Gerth and Sheryl Gay Stolberg

On Jan. 7, 1982, in a laboratory at Columbia University, a little-known science professor, Laszlo Z. Bito, finished a nine-month experiment on the eyes of cats. In his handwritten data, carefully charted in gray hardcover notebooks, lay the origins of what every pharmaceutical company longs for: a blockbuster drug.

The drug is Xalatan, a best-selling eyedrop for glaucoma. With $507 million in sales last year -- and the potential for billions more, most of it pure profit -- the four-year-old medicine is the equivalent of liquid gold for its manufacturer, the Pharmacia Corporation. The eyedrop earned Columbia University about $20 million in royalties last year, and it has made a millionaire of Dr. Bito as well.

Yet there are other, unseen, partners in the creation of Xalatan: the American taxpayers, who backed Dr. Bito's work with $4 million from the National Institutes of Health. The taxpayers have reaped no financial return on their investment; their reward, government officials say, is the eyedrop itself.

Xalatan costs patients $45 to $50 for a tiny bottle that lasts six weeks. That price -- about $1 a day for a drug that staves off blindness -- may not seem excessive. But the key ingredient in that daily dose costs Pharmacia only pennies to make, and Americans, who live in the only industrialized nation that lacks government restraints on drug prices, pay more than twice what European patients pay for the drug.

That puts Xalatan out of reach for patients like Albert Russell, a retired optician and part-time blues singer from Prince George's County, Md. Mr. Russell, whose glaucoma has left him nearly blind, lives on an $832-a-month Social Security check. He is among the one-third of elderly Americans who lack prescription drug coverage, and when he talks about Xalatan, he uses the word "outrageous" to describe its price.

To officials at Pharmacia, the price is fair. "We are bringing forth innovation," said Dr. Anders Harfstrand, the company's vice president for ophthalmology, "and innovation always brings a premium."

In this election year, the cost of prescription medicines is at the center of the political debate. With the biomedical revolution yielding a flood of new therapies, drugs are now the fastest-growing component of the nation's trillion-dollar-a-year medical bill. As Congress contemplates expanding Medicare to include prescription drug coverage, and some states move to bring drug prices more in line with those in foreign countries, the industry is struggling to fend off federal regulation that might limit its ability to set prices.

At the heart of the fight is Dr. Harfstrand's contention that the price of medication is justified by the extreme risk of failure and high cost of drug discovery -- an average of $500 million per drug, by the industry's estimate. It is an argument that the pharmaceutical industry, one of the world's most lucrative and secretive businesses, has relied on for more than 40 years. But it has rarely been put under a microscope, because the industry will not divulge the costs of researching and developing a particular drug.

To shed light on the subject, The New York Times examined Xalatan, from its genesis in Dr. Bito's laboratory to its arrival in the medicine cabinets of patients in 57 countries. Pharmacia declined to disclose specific financial information about the making of the drug. But through interviews with key participants and an analysis of publicly available documents, the examination found, among other things, that Pharmacia spent no more than $150,000 to buy the rights to Dr. Bito's invention from Columbia. Though it later spent tens of millions of its own money to develop the drug, the company acknowledges that Dr. Bito, with the taxpayers' support, provided it an "uncut diamond" that later became Xalatan.

The industry's reliance on taxpayer-supported research -- characterized as "a subsidy" by the very same economists whose work the industry relies on -- is commonplace, the examination also found. So commonplace, in fact, that one industry expert is now raising questions about the companies' arguments.

The expert, Dr. Nelson Levy, a former head of research and development at Abbott Laboratories, who now works as a consultant for industry and the federal government on drug development, bluntly challenged the industry's oft-repeated cost of developing a drug. "That it costs $500 million to develop a drug," Dr. Levy said in a recent interview, "is a lot of bull."

Finally, the examination found, federal officials have abandoned or ignored policies that could have led to lower prices for medicines developed with taxpayer dollars. That is partly because the government has lost track of what drugs are invented with its money, and partly, officials say, because the industry resisted government efforts to get involved in pricing.

As Dr. Bernadine Healy, a former director of the National Institutes of Health, said in a recent interview, "We sold away government research so cheap."

Going Against the Standard

Like many scientific discoveries, the invention of Xalatan began with a hunch. It was the mid-1970's, and Dr. Bito, a hard-driving researcher who bucked the eye-research establishment with his unconventional ideas about glaucoma treatment, had been named an assistant professor of ophthalmology at Columbia University.

Born in Budapest, he was conscripted into a forced labor coal mining camp at 18. In 1956, the year the Communists quashed a rebellion in his homeland, he escaped, eventually fleeing for the United States. His passion was writing, but he abandoned it for a career in science, particularly the study of the eye.

Dr. Bito was interested in a family of chemicals produced by the body, prostaglandins, and how they might affect the eye, particularly the fluid, known as aqueous humor, that nourishes the cornea and the lens. In glaucoma, the aqueous humor does not drain quickly enough, causing an increase in intraocular pressure inside the eye. This pressure can damage the optic nerve, causing vision loss and ultimately blindness.
An estimated two million Americans have glaucoma, and every year, 120,000 Americans go blind from the disease. The elderly, African-Americans, and people with family histories of the disease are at greatest risk. Glaucoma is often called "the sneak thief of sight." Often, by the time the patient notices vision loss, glaucoma can only be halted, not reversed.

When Dr. Bito began his research, ophthalmologists had already concluded that prostaglandins raised intraocular pressure, and were therefore dangerous. But Dr. Bito, along with a student at Columbia Medical School, Carl Camras, suspected otherwise; they thought that if prostaglandins were given in extremely small doses, they could actually reduce the pressure.

In 1977, after a series of studies on the eyes of rabbits, they published a paper showing just that. "It was blasphemy," Dr. Camras said.

Dr. Bito continued the work with monkeys, cats, and even himself, squirting the chemical in his own eye to gauge how much redness and irritation it caused. The studies were paid for by the National Eye Institute, a branch of the health institutes.

Within weeks of the cat experiment's conclusion in 1982, administrators at Columbia University had steered Dr. Bito to a patent lawyer; in May of that year, he applied for a patent.

It felt strange, he said, but it signified the changing culture of the ivory tower. As a professor, Dr. Bito was accustomed to publishing his work in journals and talking about it at scientific meetings. Patenting, to him, represented secrecy, the culture of industry, not academia.

"It was looked down on," Dr. Bito said. "It was too commercial."

Law Behind the Companies

Commerce, however, was exactly what Congress had in mind when, in late 1980, it passed legislation that directed federally financed researchers like Dr. Bito to patent their inventions, or risk losing control of them to the government.

Ronald Reagan had just won election on a platform to make America strong again. Japan's electronic industry was out-competing the United States in its own backyard. Determined not to lose, Congress passed Public Law 96-517, known as the Bayh-Dole Act after Senators Birch Bayh of Indiana and Bob Dole of Kansas.

The law was designed to push federally financed research from the university laboratory into the marketplace. Scientists who made discoveries using taxpayer money were required to file invention reports with the government. Universities were directed to license patented inventions to companies that would commercialize them.

The law was originally passed to aid small businesses, but later it was modified so that even big companies like Pharmacia could benefit. If a company did not develop a product quickly enough, the government could revoke the company's license and hand the job over to a competitor. It could also take control of an invention to alleviate "health or safety needs," the law said.

Once an invention is on the market, the law grants the government the right to buy it without paying customary royalties. At the same time, say patent experts in the Clinton administration and at the National Science Foundation, other laws enable federal agencies to put taxpayer-financed inventions out to competitive bidding. For example, the government, which buys Xalatan, could give companies other than Pharmacia the opportunity to manufacture the eyedrop and sell it at a lower price -- but only to the government.

So, these experts say, the Bayh-Dole law, in conjunction with other provisions, could result in lower drug prices for the Department of Veterans Affairs and the National Institutes of Health, two major purchasers of medicines.

But in the 20 years since the Bayh-Dole bill became law, the government has not taken advantage of these provisions, say officials at the health institutes. One reason, said Dr. Wendy Baldwin, a deputy director at the agency, is that the government already buys drugs cheaply by purchasing them in bulk. But even if federal officials wanted to use the Bayh-Dole Act to get medicines at still cheaper prices, they could not because they do not keep track of products, including drugs, that are invented with taxpayer money.

That failure has drawn criticism from the General Accounting Office, the investigative arm of Congress, which last year conducted a review of the government's invention reporting system. "Inaccurate, incomplete and inconsistent," the accounting office concluded.

Also, last year, a preliminary report by the inspector general's office of the Department of Health and Human Services found that as many as 22 percent of discoveries financed by the health institutes were not reported by universities, as is required. More than 2,000 inventions developed with government money were reported to the health institutes last year, but Dr. Baldwin and other agency officials said in interviews that they had no idea which, if any, companies had licensed those inventions, or how they were being used.

As for the issue of what consumers pay for drugs, the health institutes has concluded it should stay out of it. When Dr. Healy was director of the agency in the early 1990's, she insisted that companies interested in developing drugs that had been invented by government scientists sign contracts agreeing to "reasonable pricing" for those medicines.

The companies balked at the reasonable-pricing clause. "I was persona non grata for it," said Dr. Healy, who now heads the American Red Cross. The provision was dropped in 1995 by Dr. Harold Varmus, her successor; at the time, he said the policy was discouraging collaboration by driving industry away.

In the end, said Dr. Baldwin, the official designated by the N.I.H. to answer questions for this article, taxpayers may not get lower drug prices. Still, she said: "The current policies are actually bringing drugs to market. It's a huge advance, a wonderful accomplishment."

Going Abroad for Help

If the federal government leaves it to companies to decide how much consumers pay for taxpayer-backed inventions, universities are even less concerned about the prices. The Bayh-Dole Act has meant a windfall in revenues from licensing and royalties for them, none more than Columbia.

Last year, Columbia earned $96 million in licensing fees and royalties under the Bayh-Dole law, ranking it first among universities in royalties from inventions, said Jack Granowitz, who runs Columbia's program to commercialize university inventions. Roughly $20 million of that money was from Xalatan; one-fifth goes to Dr. Bito and the university keeps the rest.

When Dr. Bito first filed his patent application in 1982, no drug company in the United States would touch it; most glaucoma experts remembered well the studies showing prostaglandins could only hurt people with the disease. Dr. Bito recalled: "They said, 'It's crazy. You can't put prostaglandins in the eye.' "

So Dr. Bito approached another Hungarian eye researcher who knew people at Pharmacia, at the time one of Sweden's largest drug companies. (The company, now of Peapack, N.J., has since undergone two mergers, one with Upjohn in 1995, and another this year, with Monsanto.) Within a year, Dr. Bito said, Pharmacia had bought exclusive rights to his idea, paying Columbia between $100,000 and $150,000. The government received no fees; the law did not require it.

For Pharmacia, which was already marketing a cataract therapy developed by Dr. Bito's Hungarian friend, it was a nice fit. It was also a way for the company to hedge the risky bets it made on drug development.

The industry's own studies show that drug research is riskiest in the early stages, when a company has no way to tell if a given compound is a blockbuster or a dud. The companies often build on basic scientific findings that emerge from taxpayer-financed studies, underwriting the applied science themselves. But in some cases, as with Xalatan, those studies actually produce a practical discovery that can be licensed, allowing companies to step in when profits seem more assured.

No one knows precisely how many medicines result from such licensing arrangements, but they are not unusual. For example, Trusopt, a glaucoma eyedrop by Merck, was taken to the market in similar fashion, after researchers at the University of Florida, with backing from the National Eye Institute, discovered how to convert a related drug from pill to drop form. As Dr. Carl Kupfer, the institute's director, said, "A pharmaceutical company wouldn't take over the drug unless the animal testing looked very feasible."

Still, Pharmacia was hardly getting a finished product. "An uncut diamond" is how Dr. Harfstrand described Dr. Bito's work. Using the natural prostaglandins Dr. Bito had identified, Pharmacia had the task of developing a synthetic molecule that could be given safely to people.

It was a tall order. As Dr. Bito well knew from squirting the chemicals into his own eyes, the prostaglandins caused redness and irritation. One of Sweden's leading eye experts, Dr. Anders Bill, remembered informing the company that Dr. Bito's idea was "next to ridiculous," and giving it only a 5 percent chance of success. The drug industry's trade association says for every 250 compounds that emerge from a laboratory to enter this kind of pre-clinical testing, only one makes it to market.

By 1985, two years into the Pharmacia's contract with Columbia, the company's research was progressing slowly. Dr. Bito persuaded Mr. Granowitz to write a letter to the company reminding it that, under the Bayh-Dole law, the government could step in and take control of the invention. The next year, Pharmacia hired a new manager for the project, a Swedish pharmacologist, Johan Stjernschantz.

By 1988, Dr. Stjernschantz had found what Pharmacia was looking for: a family of chemical cousins to Dr. Bito's prostaglandins that also lowered pressure but without the troubling irritation. From this family, Dr. Stjernschantz said, he selected latanaprost, the key ingredient for the compound that would later take the trade name Xalatan.

The uncut diamond was now a sparkling gem.

Government's Silent Role

How much was Dr. Bito's government-supported work worth to Pharmacia? Only company officials know, and they won't say.

That kind of secrecy is typical, making it difficult for outsiders to examine drug pricing issues. Nonetheless, experts characterize work like Dr. Bito's as an extremely valuable subsidy for a business that is already receiving government help in other areas, such as tax credits for research and development.

Dr. Levy, the former Abbott Laboratories executive, says preclinical research could account for as much as 20 to 25 percent of a company's research and development budget for a particular drug.

"N.I.H.-supported research represents a subsidy to pharmaceutical development," said Dr. Louis Lasagna, an expert in drug development at Tufts University whose studies are widely cited by the industry. "But you need a midwife, the companies, to bring it to market."

The word subsidy, not surprisingly, rankles drug industry officials, who say other businesses, including the medical device industry, also benefit from public science.

Yet it is clear that the government plays an important, and an increasing, role in drug development, both through inventions like Dr. Bito's and more basic scientific research on which the companies can build. A 1995 study by the Massachusetts Institute of Technology found that, of the 14 new drugs the industry identified as the most medically significant in the preceding 25 years, 11 had their roots in studies paid for by the government.

"The general pattern is that industry is building enormously heavily on basic research supported by N.I.H.," said Dr. Francis Narin, president of C.H.I. Research, a consulting firm that has analyzed patents as a way of measuring the role public science plays in industry.

In a 1997 study commissioned by the National Science Foundation, C.H.I. looked at the most significant scientific research papers cited in medicine patents. It found that half the cited studies were paid for with United States public funds, primarily from government and academia; only 17 percent were paid for by industry. (The rest came from public and private foreign sources.)

And in a study with the National Eye Institute, published in 1996, C.H.I. found that 41 percent of patented eye-care technology was linked to research financed by the health institutes, including Dr. Bito's studies, which have been cited in 15 patents, including Xalatan's.

"I think that is very typical," Dr. Narin said of Dr. Bito's work. "If you find any good advanced biomedical patent, and you look at its science references, most of them are going to be public," meaning from publicly financed research.

The industry's estimate for the average cost of developing a drug -- $500 million -- is drawn from a study published in 1991 by Dr. Lasagna and Dr. Joseph DiMasi, an economist at Tufts, and adjusted to reflect inflation and the additional testing drug companies have begun doing to obtain F.D.A. approval for their medicines. Only a small percentage of the $500 million represents the actual cost of developing a particular medicine, Dr. DiMasi said. The rest is the cost is attributed to lost opportunities: years spent going down scientific "dry holes" and research money that could have generated interest had it been invested instead.

Dr. Levy, the drug development expert, says the Bayh-Dole law has altered that equation. In the past, Dr. Levy said, "academia was coming up with concepts, not molecules" for drug development. Today, university scientists are more commercially oriented; many are spinning off their own biotech companies to develop their ideas. That, in turn, has enabled companies like Pharmacia to shift resources away from in-house research and development and toward outside collaborations, a strategy known as "external innovation."

For instance, Pharmacia shut down Dr. Stjernschantz' prostaglandin lab after Xalatan went on the market in 1996, instead giving Dr. Stjernschantz a grant to continue his research at a nearby university. And last year, Pharmacia spent $650 million to buy Sugen, a biotech concern in San Francisco that is collaborating with the National Cancer Institute on clinical trials of its two leading drugs. The company's co-founder, Dr. Joseph Schlessinger, is a New York University scientist whose initial financing included a nine-year grant from the cancer institute, N.I.H. records show.

So the pharmaceutical companies have become more efficient, in part because university researchers are more efficient. As Dr. Levy put it, the companies are "not having to dig as many dry holes."

Drawback in Development

Once Dr. Stjernschantz had identified the latanaprost molecule, Pharmacia needed a place to produce it in large amounts for testing in people. It takes 110 raw materials, 32 separate chemical reactions and three months to make a batch of latanaprost, and few companies had the technical know-how.

Among those that did was the Chinoin Pharmaceutical and Chemical Works, in Dr. Bito's hometown, Budapest. The 88-year-old company, owned until recently by the Hungarian Communist government, sits hard by the railroad tracks in a drab corner of the city, a vast array of 100 low-slung buildings connected by a maze of steel pipes.

Dr. Bito knew Chinoin's chemists well. He introduced them to officials at Pharmacia, and after some testy east-west negotiations, clinical trials were under way by the early 1990's in three countries, with Chinoin producing the key ingredient.

Dr. Camras, the young medical student who worked with Dr. Bito at Columbia, was brought in to run the United States arm of the final study; by this time he had become an ophthalmologist, with an academic appointment at the University of Nebraska.

Human testing is typically the most expensive part of the drug development process. Clinical trials usually consist of three phases; the first study tests safety and looks for the proper dose; if the drug is safe, it moves to the second phase to test effectiveness in a limited number of patients. The costliest clinical trial is the last one, the large Phase 3 study to prove the drug is safe and effective, proof that is necessary for the Food and Drug Administration approval. Depending on the drug and the amount of medical care involved, experts say the cost of a Phase 3 trial can range from $10,000 to $20,000 per patient.

The Phase 3 study of Xalatan was relatively small, just 829 people. The company will not say what it spent on that study, or any other. But Dr. Stjernschantz, the project manager, said the total costs for all trials was significantly less than $30 million, an estimate that, a Columbia researcher said, Pharmacia provided to the university before the testing had begun.

The trials gave the company precisely what it was looking for: proof that Xalatan, given once a day, lowered intraocular pressure as much as the gold standard of glaucoma treatment, timolol.

But the studies turned up a worrisome, and unique, side effect: Xalatan caused 7.2 percent of patients' eyes to darken, changing from blue or green to brown. The company nearly pulled the plug on the project. "That was a very terrible crisis," Dr. Stjernschantz said.

In the end, the pigmentation issue led to less-than-wholehearted backing from the F.D.A., which approved the drug on June 6, 1996, with a caveat: Xalatan, it said, should be used only as backup therapy when all other drugs have failed, and not as a "first-line" treatment. It was a setback, but hardly a fatal one.

Today, Xalatan is approved for sale around the world, from the United States to Japan, Australia and all across Europe. The key ingredient is still being manufactured at Chinoin in Budapest, although the Hungarian company has since become a subsidiary of Sanofi, the French pharmaceutical giant.

The Chinoin-Pharmacia partnership has been a profitable one. Chinoin is making a 50 percent return on its prostaglandin investment, company officials said. And Pharmacia pays Chinoin slightly more than $5 million a year for the manufacturing of latanaprost, said Tibor Szabo, who directs the prostaglandin business unit at Chinoin.

That amounts to roughly one one-hundredth of Xalatan's $507 million in annual sales last year. Or, to put it another way, the cost of making the key ingredient is just 1 percent of the revenue Xalatan generates.

Pricing Around the World

Between Dr. Bito, the National Institutes of Health and Pharmacia, 20 years and many millions of dollars were spent getting Xalatan to a point where it could be sold to the public. But those costs bear little relationship to the price of the drug.

Nor is the price based on what the company spends to make and sell Xalatan, which includes not only the $5 million paid to Chinoin but also the cost of diluting, bottling and shipping the drug, the royalties paid to Columbia, and other costs, such as marketing.

Globally, there can be scores of prices for the same drug, as Xalatan shows.

In the United States, where there are no government restrictions, the basic price set by the company is determined by what the market will bear, taking into consideration the competition, the drug's side effects, and the patient population.

Xalatan is the first and only prostaglandin-based glaucoma drug, which gives it a competitive edge. It is taken only once a day; other drops must be taken more often. And aside from the eye pigmentation, it has fewer side effects. In the United States, the company sells the drug for about $36 a bottle wholesale, far more expensive than the cheapest generic, but roughly in line with other brand-name glaucoma medications, according to industry data and experts.

That price changes from customer to customer. Large health maintenance organizations, as well as the government, can often wring discounts out of manufacturers, while people with no prescription drug coverage must pay the full price. The Department of Veterans Affairs, for instance, pays $25 a bottle for Xalatan, about half what uninsured patients like Mr. Russell pay. And there are even different prices within the government; smaller federal agencies pay $29 a bottle for Xalatan.

Overseas, price controls make for a different story.

In Dr. Bito's home country, Hungary, where the government pays for approved medications, Pharmacia receives a negotiated price of $17.50 a bottle for Xalatan, said Katalin Szutrely, who runs Pharmacia's Hungarian branch. Because the drug is so costly, she said, obtaining government approval to market it was difficult. One selling point was Dr. Bito himself. "We were proud of him being the inventor," she said, "and we used his name."

That does not mean the drug is reaching a lot of patients in Hungary. A panel of Hungarian eye doctors recommended Xalatan as a first-line treatment, Ms. Szutrely said, but the government pays for it only when doctors can prove all other eyedrops have failed. As Ms. Szutrely said, "If you don't have the reimbursement, you cannot sell the drug."

Back in Washington, the debate revolves around dueling sets of statistics about why Americans often pay more. Some say the price of new medicines is driving up health care costs. Kaiser Permanente, the health maintenance organization, says it spent $4.7 million on glaucoma drugs in 1995, the year before Xalatan was introduced. Last year, Kaiser's expenditures for glaucoma reached $20.4 million, $9 million of it on Xalatan.

To counter such numbers, industry officials argue that Xalatan and other new medicines may be saving money as well, by reducing the need for doctors' visits and also for surgery. At the same time, they say the American free market provides the companies with the profits they need to plow back into research, so that patients can benefit from the next generation of drugs like Xalatan.

"I'm worried about low prices in Europe," Dr. Harfstrand said. "It discourages innovation."

And because more prescription drugs are made and sold in the United States than any other country, the thought of regulation is especially troubling to the companies. In the case of Xalatan, for instance, more than half the drug's sales are in the United States.

"The U.S. has been the only major free market for pharmaceuticals," Fred Hassan, Pharmacia's chief executive, said in a company newsletter last fall, "and that has benefited patients as well as our industry."

Science vs. Selling

As Xalatan's inventor, Dr. Bito likes to think of the drug as a triumph of science. But at Pharmacia, they speak proudly of Xalatan as a triumph of marketing.

The F.D.A.'s recommendation of Xalatan as only a backup therapy presented a considerable challenge to the company: How to persuade doctors to turn to their drug before other glaucoma medications. The company pursued an aggressive strategy, according to the drug agency's records and interviews with eye doctors, leaving the impression but not stating explicitly that Xalatan should be considered as a first-line therapy. The drug's growing sales suggest the strategy has worked; in an advertisement announcing its merger with Monsanto, Pharmacia proudly called Xalatan "the new gold standard for treatment of glaucoma."

Company documents show Pharmacia spent 40 percent of its overall revenue on marketing and administrative expenses last year, more than twice what it spent on research. In the last year alone, it increased its global sales force by 30 percent to 6,500 people, including scores of "detail men" who make door-to-door visits to doctors. Last year, company officials say, those detail men gave away more than a million free samples of Xalatan to doctors.

Companies gauge a product's success by its gross-profit margin -- the money left from sales after expenses, but before taxes. The Pharmaceutical Research and Manufacturers Association says only three out of 10 medicines recover their research and development costs. But those that do, like Xalatan, can be hugely profitable.

A reconstruction of Xalatan's profitability, based on outside experts and company documents, suggests its profit margin is likely higher than the company's average of 76 percent, perhaps as high as 90 percent. The company, however, will not talk about Xalatan's earnings.

As Dr. Harfstrand said, "We never comment on gross margins on individual products."

Easy and Effective

To spend a day in the examining room with Dr. Harry Quigley, director of the glaucoma service at the Wilmer Eye Institute at Johns Hopkins University, is to see why Xalatan is popular with both doctors and patients. As one of the nation's best-known eye specialists, Dr. Quigley sees as many as 40 patients on any given day, and these days, it seems, he is prescribing Xalatan to most.

He likes the drug for the obvious reason: It reduces intraocular pressure. His patients like it, too; in interviews, several said it caused less redness and irritation than other glaucoma drops, and they preferred its once-a-day formula. Other drugs to combat glaucoma must be taken as often as four times a day. For Dr. Quigley, convenience is hardly a side issue; the once-a-day regimen, he said, means patients are more likely to take their eyedrops.

In October of 1996, a few months after Xalatan was on pharmacy shelves, Dr. Quigley prescribed it to Mr. Russell, the retired optician, who is blind in his right eye and nearly blind in the left. The drug worked to perfection, lowering Mr. Russell's intraocular pressure to well within normal range. "It was fantastic," he said.

The only problem was the price. "Forty-five bucks," Mr. Russell exclaimed, cradling a bottle of Xalatan in his hand. "I flinch every time I think about it."

Like many older people, Mr. Russell takes other medications that run up his monthly prescription drug bill. For a time, he said, he paid out of pocket for Xalatan. Then his wife, Millie, discovered that Pharmacia runs a prescription assistance program for patients with "short-term financial hardship." Under the program, the company provides drugs, with patients typically making a $5 co-payment to the pharmacy, for six months, and then patients can reapply.

Mr. Russell was approved for the program. But last August, he received a letter from Pharmacia telling him his discounted supply of Xalatan would run out in November, and urging him to find another, more permanent, way to pay for the drug.

But Mr. Russell did not have another way to pay. So Dr. Quigley proposed an alternative that Medicare would pay for: surgery to lower the intraocular pressure. It was not the optimal solution, Dr. Quigley said, because Mr. Russell's glaucoma was well controlled with the drops and the operation meant a two to three percent risk that he would lose sight in his only good eye, plus a continuing risk of infection.

"The best way to take care of Mr. Russell would have been to continue his medications," the doctor said. "That was not practical, so we did the next best thing."

For Dr. Quigley, the situation was hardly extraordinary. Too many of his patients, he said, are "being forced to choose between paying the rent, buying food and taking expensive medicine." And he is irritated that Pharmacia offers patients only short-term help. "If somebody is going to start taking medication," he said, "they are going to need it indefinitely, and they are unlikely to be poor for only 6 or 12 months."

Also troubled is Dr. J. William Doyle, a University of Florida ophthalmologist who has studied company assistance programs and found them often inaccessible to patients. "It's a hassle," he said, and many patients choose cheaper, less effective medicines rather than jumping through the bureaucratic hoops necessary to get drugs at reduced prices.

At Pharmacia, officials will not divulge information about how many patients receive help from the medication assistance program, or how much the company spends on in it.

Mr. Russell, for one, says he is quite familiar with the pharmaceutical industry’s arguments about the cost of prescription drugs, and he does not believe them.

"They say the extra price is for research," he said. "That’s hard to believe."

Though it is not the most often-prescribed glaucoma drug, Xalatan brought in more revenue last year than any of its competitors, and was Pharmacia’s best-selling product prior to the company’s merger with Monsanto. Pharmacia, which had $7 billion in revenue last year, before the merger, forecasts $750 million in annual sales for Xalatan by 2002. But the patent is due to expire in 2011, according to the company, and competitors are busy developing rival products. Pharmacia is busy, too; it is already seeking F.D.A. approval of a new product, a combination of Xalatan and timolol, the leading generic competitor, that could extend the life of the patent.

As for Dr. Bito, he has closed down his lab at Columbia and is back in Budapest, living in a spacious apartment with high ceilings and wood floors and a large picture window that looks out on the Roman Catholic church he attended as a boy. Despite the millions he has earned from Xalatan, he lives relatively modestly, driving around hills above the Danube in an 18-year-old Russian car. He has finally achieved his dream of becoming a novelist; his latest book, "Abraham & Isaac," has made the best-seller list in Hungary.

The Boston Globe

April 5, 1998

Public handouts enrich drug makers, scientists

By Mitchell Zuckoff, Alice Dembner, Matt Carroll

Working in a public laboratory, backed by $ 3.2 million in federal grants, Dr. Barry S. Coller turned a scientific hunch into a "super aspirin" and turned himself into a Park Avenue multimillionaire.

Coller's royalties from the sale of ReoPro, an intravenous drug that prevents blood clotting after angioplasty, are expected to hit $ 6.4 million by summer. The drug manufacturer, analysts say, will make a 28 percent profit. Heart patients get a new treatment. But the taxpayers who underwrote the development of ReoPro and scores of other new drugs get next to nothing.

Some, like Eric Harrington, can't even afford the new drugs.

To control Harrington's multiple sclerosis, his doctor would like to prescribe Avonex, a drug developed by Cambridge-based Biogen and tested with $ 4.6 million in government aid. But Biogen charges more than $ 11,000 for a year's supply. And Harrington, a maintenance foreman with no prescription coverage, doesn't have $ 900 a month for medicine.

"They take my tax dollars, it benefits the companies and I don't get any use out of it," said Harrington of Arlington.

Tracking government-funded research to develop new treatments, a Spotlight team investigation revealed a billion-dollar taxpayers' subsidy for pharmaceutical companies already awash in profits. The investigation also documented a pattern of scientists and universities cashing in on government-funded inventions.

The government spending helps bring new drugs to the public. But taxpayers often end up paying onerous prices at the pharmacy for medicine their tax dollars helped to create.

Now Congress is preparing to increase the stakes by doubling the budget for the National Institutes of Health, the main dispenser of grants for medical research. Scientists and drug companies are cheering, since NIH money comes with few obligations, like a bank loan that never comes due. In fact, NIH only loosely tracks its spending on new drug development and rarely asks for any return of taxpayers' seed money.

Coller declined to comment on his research-to-riches story. Drug industry leaders say that NIH -funded research lays important groundwork for drug development, and they argue that restricting access to that work would delay development of new drugs essential to the health of Americans. Underscoring that point, Biogen president Jim Tobin said that without NIH's support, the company "would have taken a pass" on Avonex. But he and others also argue that to focus on NIH's investment is to ignore the much larger outlay by pharmaceutical and biotechnology companies themselves.

"This is a wonderful synergy that has great benefit for patients with medical needs," said Judith H. Bello, executive vice president of the Pharmaceutical Research and Manufacturers of America (PhRMA). "We don't want to erect deterrents to that collaboration."

But critics ask why an industry that generates net profits more than twice as large as those of other major US businesses gets taxpayer assistance with so few strings attached.

"Taxpayers' money ought to earn money," said William Haddad, chairman of Mir Pharmaceuticals, a generic drug manufacturer, who believes that companies with successful products should reimburse the government.

The federal Department of Energy already requires payback of research funds in similar situations, and some prescription drug companies endorse the concept of a partial reimbursement through royalties to NIH. But the majority of the industry supports the status quo and vehemently opposes a plan proposed by US Representative Bernard Sanders of Vermont to cut the prices of drugs developed with public money. Sanders calls the current system "an outrageous example of corporate welfare."

The Spotlight team investigation of that system found:

- 45 of 50 top-selling drugs got government subsidies totaling nearly $ 175 million. The single largest public investment was $ 45.9 million for the cancer drug Proleukin. The drugs selected for study were the bestsellers among those the Food and Drug Administration deemed most important or unique. The Globe studied 35 new drugs and 15 "orphan" drugs, for rare diseases, approved by the FDA since 1992.

- The average net profit margin of the companies making those drugs was 14 percent in 1997, more than double the 6 percent average for industrial companies in the Standard & Poor's 500.

- NIH spent at least $ 1 billion on drug and vaccine development in fiscal 1996, but took in only $ 27 million in royalties from all products. By funding the early stages of research and testing, NIH assumes great risk while reaping few financial rewards.

- NIH is supposed to protect the public's investment by monitoring the products it helped develop. But in some cases, NIH officials can't even determine if the agency contributed to the development of a drug.

Unlike most developed nations, the United States has no national drug policy, so there is no overall direction, no coordination, and no evaluation of the costs and benefits of federal spending for drug development, according to Stephen W. Schondelmeyer, a professor at the University of Minnesota's College of Pharmacy.

The industry takes full advantage of the situation, building on NIH's basic and applied research and readily accepting the government's help in testing new drugs.

As a result, researchers like Coller are striking it rich with tax dollars. Robert A. Holton, a professor of organic chemistry at Florida State University, received about $ 2.3 million from NIH to help develop a synthetic form of the cancer drug Taxol. Last year, he got $ 11 million in royalties on the semi-synthetic Taxol, bringing his total since 1993 to nearly $ 25 million. The NIH money, he said, was "key" to his work.

Private companies are piggybacking on government research. Chiron Corp. of

California charges kidney cancer patients up to $ 20,000 for treatment with Proleukin. The drug won FDA approval after nearly $ 46 million worth of clinical tests conducted or funded by NIH.

Corporations are getting direct government handouts. NIH awarded Abbott Laboratories of Illinois $ 3.2 million to design and develop a new drug, called a protease inhibitor, to slow the progression of AIDS. Abbott sold $ 41 million worth of Norvir in the first half of 1997.

Even foreign companies are cashing in. Teva Pharmaceutical Industries of Israel sold about $ 50 million worth of its multiple sclerosis drug, Copaxone, in the United States last year, reaping the rewards of nearly $ 5 million NIH and the FDA spent to help test it.

"They're NIH in the business of pouring money into private industry and failing to keep track of it," said professor Michael H. Davis, a specialist in intellectual property at Cleveland State University College of Law. "We're talking about millions of dollars wasted and about people being exploited because of excessively high drug prices."

NIH director Harold Varmus defends the agency's actions, asserting that they fit its goal of supporting research and ensuring that potential products are developed.

"The process is designed to benefit both the public good and private industry, and it works well," he said in a written statement.

"I do not attempt to measure the role of NIH in drug development by comparing how much money we spend on research with royalty revenue we generate," he added. "Royalties are subservient to public health considerations."

Rights to discoveries ceded by Congress

Up until the 1980s, the government owned the rights to any discoveries made with federal aid. But concern that important new drugs and other products discovered with federal assistance were not making it to market led Congress to change the rules. In a series of laws, Congress gave away the government's rights - and the ensuing profits - to universities, nonprofit laboratories, and small businesses.

In addition, Congress ordered federal laboratories to cooperate more closely with industry in developing new treatments and products, and gave federal scientists an incentive by allowing them to collect royalties on inventions made while on the federal payroll.

To protect the public's interest, the law ordered federal agencies to ensure that products developed under the new system were "reasonably" available to the public and required them to collect royalties for work performed by government scientists that led to new patents. But in practice, the system has authorized loosely supervised government subsidies that go far beyond NIH's boost to the pharmaceutical industry, extending from other federal agencies to the fields of electronics, defense, and energy, among others.

Without doubt, the system has spurred economic development, added jobs, and generated tax dollars. The subsidies and results are striking in the pharmaceutical industry, where there has been an explosion of new drugs, many of which save lives and reduce hospitalization.

But even as he praises such advances, one of the architects of the new system, former US senator Birch Bayh, an Indiana Democrat, worries that they are being tainted by price-gouging or profiteering.

"How do we deal with a situation where one person who has a new mousetrap that is a lifesaver is gouging the public?" asked Bayh, who is now a lobbyist. "If there's a formula we can find for reasonableness, then we should do that."

In addition, by giving up its share of the profits, the government is losing a source of revenue that could be tapped, instead of taxes, to pay for more research.

That drain occurred during a decade that saw a doubling of NIH's budget. Now, President Clinton is proposing an additional 50 percent increase over the next five years, and congressional leaders in both parties want to top that, advocating a 100 percent increase that would bring NIH's annual budget to $ 26 billion.

Massachusetts would benefit greatly from an expansion of NIH's coffers, since the state's prestigious researchers win about 10 percent of NIH grants. But some specialists worry that the money would give NIH less incentive to track its spending on drug development and end up sending more money into the pockets of individual researchers and big pharmaceutical corporations.

Industry leaders see no downside to that development, even as they downplay the importance of NIH's contribution.

"The vast majority of new medicines are actually developed by companies," said Jeff Trewhitt, a PhRMA spokesman. " NIH does most of the basic discovery work, but we do the applied research. We take new medicines through the expensive process of clinical testing and FDA approval. The cost per product can be up to $ 600 million."

Trewhitt acknowledges that the $ 600 million figure is an extrapolation, adjusted for inflation and changes in research and development, based on a disputed Tufts University study that pegged the average cost of developing a drug at $ 231 million in 1987. Both numbers count not only company spending but money lost on unsuccessful drugs and the expense of using funds for drug development rather than some other purpose. A 1993 government study that used the same base figures, however, found that the out-of-pocket costs after tax breaks were just $ 65.5 million. None of the figures can be verified because companies refuse to release actual expenses for individual drugs.

Regardless of the actual cost, critics agree with Trewhitt thvelopment.

But Coller has also served himself - and the drug companies that produce and sell his drug.

Coller, a doctor who specializes in the study of blood, developed his anti-clotting drug in the labs of the State University of New York at Stony Brook, where he was a member of the faculty. He credits SUNY for providing "an enriched scientific environment" and the National Heart, Lung and Blood Institute, a branch of NIH, for funding the basic work. Over nearly 20 years, NIH records show that the agency contributed $ 3.2 million to his efforts.

But after testing the developing drug in animals, Coller and SUNY turned to industry in 1986. They sold the rights to develop ReoPro to Centocor, a young biotechnology company from Malvern, Pa. Over the next eight years, Centocor would supplement Coller's NIH research funding and his state salary, while also giving SUNY more than $ 1 million in licensing fees and upfront royalties. Centocor paid to patent the drug and says it spent more than $ 200 million on development.

ReoPro won FDA approval in late 1994. Given intravenously to patients following surgery for clogged arteries, the drug helps prevent heart attacks from blood clots. Eli Lilly and Co. markets ReoPro for Centocor. In 1997, annual worldwide sales hit $ 254 million.

Under the deal with Centocor, the university collected nearly $ 12 million in royalties by the end of 1997 and expects another $ 4 million by summer, much of which will fund university research. Coller's share will be $ 6.4 million. Analysts predict sales will nearly triple by 2001, which could boost Coller's royalty income over $ 20 million.

A year before ReoPro won FDA approval, Coller departed SUNY for Mount Sinai Medical Center in Manhattan, becoming chairman of medicine, its largest department. He purchased a home on Park Avenue that realtors say is worth more than $ 1.5 million.

Coller declined to discuss whether taxpayers beyond the sphere of the state university deserve a share of his success, while a Centocor spokesman said the company played by the rules.

Officials at SUNY said NIH does not deserve a dime back. "The university takes on all the responsibility of patenting and marketing and trying to develop the invention," said John Petersen, director of the university's office of technology licensing. "The public as a whole benefits from getting the product on the market."

But not all scientists agree that is sufficient at current drug prices. ReoPro costs about $ 1,500 per treatment.

"When the public pays for something, they should expect to get access to it," said Richard J. Roberts, a Nobel laureate in medicine who is now research director of New England Biolabs in Beverly. "They're not expecting that a university or a university researcher is going to get rich on it."

But Coller has plenty of company in the millionaire's circle.

Royalties for Holton, the Florida State professor, dwarf Coller's. For his work developing the semi-synthetic form of Taxol, Holton says he's collected just shy of $ 25 million in royalties.

"In 1983, when I first started working on Taxol, I never expected it would be a drug," said Holton, who still teaches organic chemistry. Over 12 years, he received $ 2.3 million from NIH for work that changed his view.

While scientists at the National Cancer Institute, another branch of NIH, were spending nearly $ 27 million to develop and test the natural form of the drug, derived from the bark of Pacific yew trees, Holton pressed ahead with his search for a cheaper and more readily available source. His success boosted the sales of Taxol and added to the revenues of Bristol-Myers Squibb, which produces and sells the drug. In the first half of 1997, Bristol-Myers sold $ 323 million of Taxol in the United States, helping to push its profit margin to 19 percent.

Holton says he'd be willing to give a share of his royalties to NIH "as long as it went back to the NIH budget in the same area that generated it and didn't supplant other funds."

For its part, Bristol-Myers last year made its first - and only - royalty payment to NIH for Taxol, $ 3.4 million in exchange for additional rights that extend Bristol-Myers's monopoly on the drug. The payment followed years of criticism of the original deal in which the government gave the company rights to Taxol without seeking any direct payback.

Bristol-Myers spokeswoman Jane Kramer says the public got much more than the royalties, including "a cancer-fighting drug that it wouldn't otherwise have had," and NCI got free supplies of Taxol, research support to test the drug for new uses and royalties that together were worth $ 30 million.

But critics say the payments don't begin to compensate taxpayers. "It's a great deal for Bristol-Myers, but it's a terrible deal for the taxpayers," said James P. Love, an executive with the Taxpayer Assets Project, founded by Ralph Nader. "It's as if the government hired 1,000 people to build cars for General Motors and GM agreed to pay for their coffee."

Like Bristol-Myers, other private companies are riding government research to the bank. Chiron Corp. of Emeryville, Calif., for example, is the beneficiary of more than $ 45 million worth of clinical tests conducted or funded by NIH.

The company sells Proleukin, a genetically engineered form of interleukin-2, for the treatment of kidney cancer and malignant melanoma. The substance was patented by scientists at Cetus Corp., later taken over by Chiron. But it was work by surgeon Steven A. Rosenberg and his colleagues at the National Cancer Institute that showed the drug could help people with advanced kidney cancer. And it was NCI that funded most nationwide tests of the drug for use in other cancers. NCI eagerly shared the results of its work while asking little in return. Rosenberg, who favors such no-strings interactions among scientists, declined comment about the financial aspects of interleukin-2.

Maurice Wolin, medical affairs director for Chiron, acknowledges Rosenberg's contribution. But he says Chiron poured millions of dollars into the drug, and provided it free to Rosenberg and his patients. Added Chiron vice president James Knighton, "All the constituents get a share that's fair to the risk they bore."

Knighton said Chiron sold more than $ 75 million of Proleukin worldwide in 1. NIH said it gets no royalties.

NIH spent $ 1 billion on drug research in 1996

Rosenberg's years of work on Proleukin are indicative of the government's massive investment in developing new medicines that goes far beyond grants to university researchers.

In fact, NIH has several divisions devoted to searching for potential drugs. For certain illnesses, government scientists also run a screening service for drug companies, spending taxpayer dollars to determine whether those companies have a potential winner among the chemical substances they've patented. The companies retain all rights and profits.

NIH says it spent approximately $ 1 billion on drug and vaccine development in fiscal 1996. But the actual figure may be higher. NIH largely tracks its spending by disease, not by drug. For most drugs, therefore, NIH has no idea how much taxpayers invested and no way to determine if they're getting a fair return.

"Every time we've tried to work backwards, the picture gets very complex of how a drug or compound was created," said Barbara McGarey, deputy director of NIH's Office of Technology Transfer.

The Spotlight team calculated government spending on 50 drugs by conducting its own search of NIH's grant database, a method that probably underestimates taxpayer contributions since the database does not include all work done by NIH's own scientists and often does not specify drug names. Still, the total spent on those 50 drugs from 1972 to 1996 was just under $ 175 million. Hundreds of millions more were undoubtedly spent on scores of other drugs approved by the FDA during that period and on drugs still in the pipeline.

NIH also does little to enforce rules designed to protect US rights to drugs that result from taxpayer-funded work.

For example, government rules require recipients of NIH money to report any inventions that resulted and to acknowledge the federal role in any patent received. But, when asked by the Globe, NIH could not produce any reports on five specific drugs developed with millions of dollars from NIH. The agency says there is neither time nor resources to verify researchers' compliance with the rules, despite a warning from its own inspector general in 1994 that NIH's lax enforcement meant the agency was "not able to protect the taxpayers' interest."

As a result of federal policies and practices, NIH's royalty income is small. In fiscal 1996, the year NIH says it spent $ 1 billion on drug development, it took in just $ 27 million in royalties from all products that came out of its research. NIH does not tally its drug royalties separately.

NIH royalty revenue is rising - it hit $ 35 million in 1997 - and would be expected to lag development spending, but it is dwarfed by some universities' royalties. The University of California, for instance, collected $ 57 million in 1996.

In most cases, NIH refuses to release royalty totals from specific drugs, saying that would reveal proprietary information about private companies. But NIH's typical royalty rates are lower than those usually negotiated by universities and firms.

McGarey said NIH aggressively pursues royalties. But she acknowledged, "We license with an eye toward commercializing the product for a reasonable return on the public's investment. Our primary goal is not to maximize the financial return."

NIH says a similar philosophy drives its policy that allows private companies to compete with university researchers for grants. Seven percent of all NIH research grants and contracts in 1997 - $ 733 million - went to for-profit organizations.

Abbott Laboratories, for example, won $ 3.2 million in grants from 1988 to 1992 that laid the groundwork for its development of Norvir, a protease inhibitor used to fight the progression of AIDS. In 1992, the Illinois company began testing Norvir in animals, followed by tests in patients with additional help from NIH. The FDA approved it for market in 1996. US sales of the drug, typically used as part of a two- or three-drug "cocktail," hit $ 41 million in the first half of 1997. The company reported a profit margin of 18 percent.

As required, the company credited the NIH grant on its patent for Norvir. But NIH didn't ask for any financial return and Abbott didn't offer. Abbott officials declined comment.

Foreign-based firms also benefit from US subsidies

The government's subsidy of drug companies also extends abroad. Twenty of the drugs examined by the Globe were developed by foreign-based firms that benefited from NIH or FDA-funded research or testing. The subsidy totaled $ 39 million.

Teva Pharmaceutical Industries of Israel, for example, won FDA approval to sell its multiple sclerosis drug, Copaxone, with the help of about $ 4.9 million worth of testing funded by NIH and the FDA. The saga began when researchers in Israel working independently of Teva discovered the drug. They sought help from colleagues in New York, who won more than $ 4 million in NIH grants to try the drug in patients. Armed with successful results, the Israeli researchers licensed the drug to Teva. The company then received $ 300,000 more to test Copaxone from the FDA's orphan drug program, which offers grants, tax breaks, and a seven-year monopoly to companies developing drugs for rare diseases.

Analysts estimate Teva sold $ 50 million worth of Copaxone in 1997, the first year the drug was available in the United States. Teva manufactures the drug in Israel and markets it here through a joint venture with another company. After taxes, profits are sent back to Israel. Patients pay more than $ 10,000 a year for the drug, which reduces MS symptoms.

Teva officials say the company would be willing to pay back similar grants in the future if that were required, especially if the funds were recycled for other research projects. But they note that the Copaxone grants were not awarded with any strings.

"It's a public ripoff," said patent lawyer Michael Davis, who represented citizens in a suit over drug pricing. "Our government is more than eager to allow public research to be siphoned off to foreign companies. So we're not only paying twice, we're paying it to a foreign company."

That seems the ultimate injustice to Eric Harrington as he struggles with multiple sclerosis. His most recent bout numbed his entire body, at its worst leaving him unable to hold a cup of coffee, let alone feed his newborn daughter. By early February, he had exhausted his vacation time and all but one sick day for 1998.

Back at work now, he is increasingly worried that he will lose his job at a local real estate company. His wife, Anne, fears that his next episode will leave him unable to walk unassisted. The irony is that if he becomes unemployed or disabled, he might qualify for Medicaid or Medicare coverage that would pay for a drug to ease his symptoms.

Biogen, which makes Avonex, the MS drug Harrington's doctor prefers, has offered to discount the drug, but Harrington says it is still out of reach. The company reported a net profit of $ 89 million in 1997. Teva, which sells the competitor drug Copaxone, made $ 101 million.

"The bottom line is that taxpayers invested when no one else would," said Ralph DeGennaro, executive director of Taxpayers for Common Sense, a budget watchdog group. "It's only fair that they get a cut when the pharmaceutical companies hit the jackpot."

Private profits from public funds

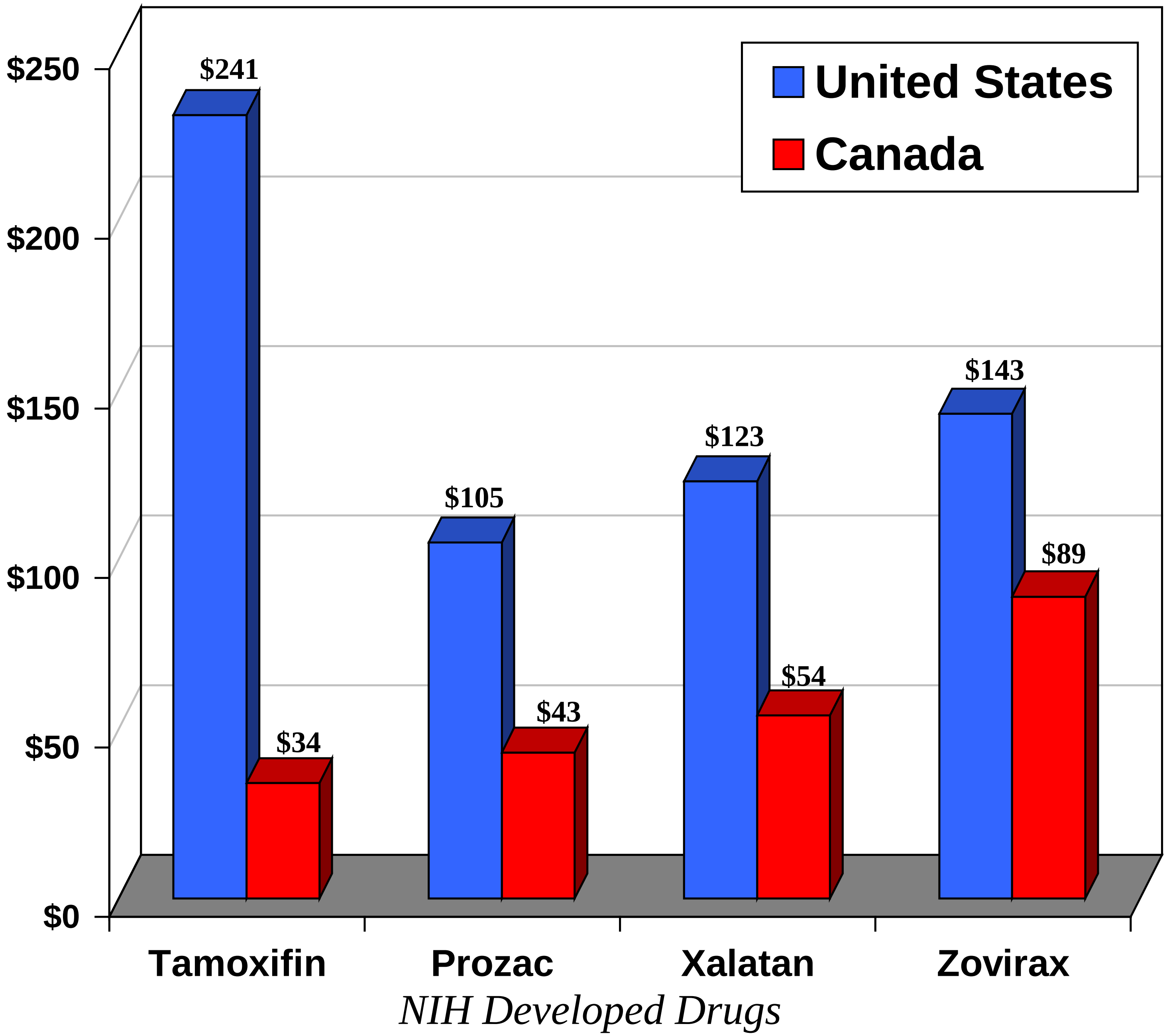
The drug industry, which is twice as profitable on average as other major businesses in the United States, benefits from substantial government subsidies obtained through grants to academic or government researchers or given directly to the companies themselves.

The Globe looked at 50 top-selling drugs approved by the Food and Drug Administration over the past five years: 35 new drugs, which are bestsellers among those the FDA deemed most important or most unique, and 15 "orphan" drugs targeting rare diseases. Thirty-three of the 35 new drugs and 12 of the 15 orphans received money from the National Institutes of Health or the FDA to help in discovery, development, or testing.

Appendix

UNREASONABLE PRICES

Taxpayers Get Fleeced on Drugs They Paid to Develop



Other Resources

Rep. Sanders Prescription Drug Website

http://bernie.house.gov/prescriptions

Joint Economic Committee Report – NIH

http://www.senate.gov/~jec/nih.pdf